Remarks

Claims

Claims 1-15 and 32-68 are pending in the application.

Claims 2, 4, 7, 10-14, 32-54, 56-58, 60-61, 63, 66-70, 72-75, 77 and 79-82 are withdrawn from consideration.

Applicants herewith amend no claims, delete no claims, or add no new claims.

Therefore, Claims 1, 3, 5, 6, 8, 9, 15, 55, 59, 62, 64, 71, 76 and 78 are currently pending in the application.

Rejection of Claims Under 35 U.S.C. § 102/103

The Office Action has rejected claims 1, 3, 5, 6, 8, 9, 15, 55, 59, 62, 64, 65, 76, and 78 as allegedly being anticipated under 35 U.S.C. § 102(b) or, in the alternate, allegedly being obvious under 35 U.S.C. § 103(a), by U.S. Application Publication No. 2001/0007747 A1 (hereinafter "Bochkariov"). Applicants respectfully traverse these rejections.

Present claims 1, 3, 5, 6, 8, 9, 15, 55, 59, 62, 64, 71, 76 and 78 are drawn to compositions or kits comprising two or more different, modified, monomeric deoxyribonucleotide triphosphates or reaction mixtures comprising nucleic acid molecules having 2 or more different, modified, monomeric deoxyribonucleotide triphosphates.

Rejection of Claims Under 35 U.S.C. § 102

An anticipation rejection under 35 U.S.C. § 102 requires a showing that each limitation of a claim is found in a single reference, practice or device. See Kalman v. Kimberly Clark Corp., 713 F.2d 760, 771 (Fed. Cir. 1983), cert. denied, 465 U.S. 1026 (1984). See also M.P.E.P. 8th ed., § 2131 (rev. 2, May 2004) ("To anticipate a claim, the reference must teach every element of the claim.").

The Bochkariov reference does not teach compositions, kits or reactions mixtures that include all of the limitations encompassed by the currently presented claims. The Action states, at Item 7, "Bochkariov et al., paragraph [0011] disclose kits and related methods for use in labeling nucleic acids." The Office Action further states, at Item 10 and 11, "Bochkariov et al.,

paragraph [0049] disclose kits and states explicitly that the kit may "functionalized nucleotides", dNTPs and/or rNTPs, labels, as well as a variety of reagents. The presence of "functionalized nucleotides" and "dNTPs" is deemed to teach the limitation of having "2 or more" different, modified, monomeric deoxynucleotide triphosphates (dNTPs) in a composition." However, Bochkariov fails to disclose compositions, kits and/or reaction mixtures as currently recited in independent claims 1, 55 and/or 76, respectively. In particular, Bochkariov does not teach compositions or kits "comprising 2 or more different, modified, monomeric deoxyribonucleotide triphosphates" or reaction mixtures "comprising nucleic acid molecules having 2 or more different, modified, monomeric deoxyribonucleotide triphosphates" as currently claimed.

The labeling methods employed by Bochkariov involve the use of **a single (or the same type of)** modified monomeric deoxyribonucleotide triphosphate. This is in contrast to the present composition and kit claims that comprise **2 or more different**, modified, monomeric deoxyribonucleotide triphosphates and/or the reaction mixture claims that comprise nucleic acid molecules having **2 or more different**, modified, monomeric deoxyribonucleotide triphosphates. More specifically, Bochkariov's labeling compositions and methods involve the use of a single type of nucleotide analog (e.g., allylamino-dUTP, also referred to as AA-dUTP) for labeling nucleic acid molecules within the same reaction, whereas in the instant case, the compositions, kits, and reaction mixtures involve the use of at least two different modified, monomeric deoxyribonucleotide triphosphates (e.g., AA-dUTP and AH-dATP). See, for example, Example 1, paragraph [0128] in Bochkariov and Example 1, paragraph [0055] in the instant case.

The Action asserts that at paragraph [0026], Bochkariov discloses compositions that "may comprise a plurality of modified nucleotides including those that are capable of binding one or more labels." See Action at page 3. However, regardless of the ability of Bochkariov's preferred "nucleotide analogs of interest" to bind multiple labels, Applicants fail to see any reference to the use of a plurality of different, modified nucleotides within the same composition, kit or reaction mixture anywhere in Bochkariov. This lack of any disclosure can not be remedied by Bochkariov paragraph [0018] stating that "In this specification and the appended claims, the singular forms of "a," "an" and 'the" include plural reference unless the

context clearly dictates otherwise. Thus, Bochkariov does not anticipate the present claims and Applicants therefore respectfully request that the Examiner withdraw the present rejection.

In conclusion, Bochkariov does not teach compositions or kits comprising 2 or more different, modified, monomeric deoxyribonucleotide triphosphates or reaction mixtures comprising nucleic acid molecules having 2 or more different, modified, monomeric deoxyribonucleotide triphosphates as is presently claimed. Thus, Bochkariov does not anticipate the presently claimed compositions, kits and/or reactions mixtures and Applicants request that the rejection of claims 1, 3, 5, 6, 8, 9, 15, 55, 59, 62, 64, 65, 76, and 78 under 35 U.S.C. § 102(b) be withdrawn accordingly.

Rejection of Claims Under 35 U.S.C. § 102/103

The Office Action has also rejected claims, in the alternate, as allegedly being obvious under 35 U.S.C. § 103(a), by U.S. Application Publication No. 2001/0007747 A1 (hereinafter "Bochkariov"). Applicants are not clear as to what other reference(s) or teaching(s) are combined with Bochkariov reference to arrive at this conclusion by the Office. Applicants traverse the rejection and argue as follows.

In order to show obviousness under 35 U.S.C. 103(a), the combined references must provide all the elements of the claimed invention. Obviousness under 35 U.S.C. 103(a) is determined with respect to the subject matter as a whole, and requires inquiry into several elements. As set forth by the Supreme Court in Graham v Deere Co., 383 U.S. 1 (1966), and as re-affirmed in KSR International Co. v. Teleflex Inc., 550 U.S. 398 (2007), an obviousness inquiry includes 1) determining the scope and contents of the prior art; 2) ascertaining the differences between the prior art and the claims at issue; and 3) resolving the level of ordinary skill in the pertinent art. In addition, secondary considerations may be taken into account.

Applicants submit that the level of skill in the pertinent art is high, as the practitioners in the art are often highly educated and skilled scientists with experience in the relevant art.

As argued above, the Bochkariov reference teaches using a single type of nucleotide analog and then a single dye to label it. Bochkariov does not teach, or disclose use of two or more modified nucleotides and two or more dyes to label these modified nucleotides. Nor

does Bochkariov realize the advantages such an approach may offer. For example, Applicants disclose the advantages of such an approach in the specification at page 5, paragraphs [0013] and [0014]:

> **[0013]** Thus, by incorporation of different labels (two or more) into a nucleic acid molecule, the invention may provide more sensitive probes since the different labels have different attributes and characteristics and those different characteristics and attributes can be used to facilitate detection of the probe. In another aspect, different nucleic acid molecules or different populations of nucleic acid molecules may be differentially labeled in accordance with the invention. Thus, by incorporating different labels into different nucleic acid molecules (or populations thereof), the invention provides different probes which can be differentially detected based on the characteristics and features of the labels used. In one example, a population of nucleic acid molecules from one tissue or cell (e.g. mRNA molecules) may be labeled with one detectable label while a second population of nucleic acid molecules from a different cell or tissue may be labeled with a second detectable label. Such differential labeling should allow for simultaneous detection and analysis of multiple nucleic acid samples, thus reducing costs and increasing throughput. For example, a combination of different probes having different labels can be reacted on an array and the gene expression profile can be determined for each different sample based on the label detected.
>
> **[0014]** In yet another aspect, a number (two or more) of different nucleotides may be incorporated into one or a number of different nucleic acid molecules to facilitate labeling of those nucleic acid molecules. In accordance with the invention, the use of multiple (two or more) modified nucleotides during synthesis of a nucleic acid molecule may increase the number of a ratio of incorporated modified nucleotides, labeling such modified nucleotides should therefore provide a probe having a higher amount of ratio of labels, thus producing a more sensitive probe for detection. As noted, such labeling may be accomplished with two or more different detectable labels depending on the need.

Furthermore, there is no motivation in the Bochkariov to combine its teachings with skills available in the art or other knowledge available in the art at the time of the instant

invention. Therefore, Applicants respectfully submit that at least for these reasons the obviousness rejection in view of Bochkariov should be withdrawn.

Conclusion

Applicants have made an earnest effort to place their application in proper form for examination and allowance. In view of the foregoing, Applicants respectfully request reconsideration of this application.

Respectfully Submitted,

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